

# A design for process-outcome psychotherapy research in adolescents with Borderline Personality Pathology

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## ARTICLE INFO

### Keywords:

Psychotherapy process  
Borderline personality pathology  
Process-outcome  
Alliance  
Psychophysiology  
Early intervention

## ABSTRACT

Underage patients with Borderline Personality Pathology (BPP) are in need of specialised psychotherapeutic treatment. A handful of these treatments, including Adolescent Identity Treatment (AIT) and Dialectical Behavior Therapy for Adolescents (DBT-A), have been adapted for adolescent patients. Psychotherapy research has shown that the outcome of different psychotherapeutic approaches can be very similar despite conceptual and practical differences between the theoretical models. Therefore, to understand what really works in psychotherapy, it is necessary to investigate the psychotherapeutic process and its effects on the patient.

This paper presents a study design for process-outcome research, integrating (1) a classical outcome design, comparing AIT and DBT-A in a non-inferiority trial assessing changes in psychosocial functioning at 12 months after baseline as primary outcome; and (2) a process research design, addressing multiple BPP and psychotherapy relevant factors. These factors include well-studied generic variables such as the psychotherapeutic alliance, more recent approaches such as video-based identification of significant therapeutic events, as well as more experimental approaches such as psychophysiological markers measured during the therapeutic sessions.

The use of repeated measures and the methodological pluralism which includes event and micro-process analyses has been recommended for psychotherapy research aiming at a better understanding of the interplay of factors at work to narrow the gap between research and practice in this field.

## 1. Introduction

It is important to diagnose personality disorders (PD) already in adolescence [1–3]. Tackett et al. [4] have outlined the usefulness of a life span perspective on personality pathology from early childhood to later life. Reliability, validity, temporal stability and prevalence of the borderline personality disorder (BPD) diagnoses in adolescents are similar to those in adulthood [5–7]. The prevalence of BPD in adolescents is estimated between 1 and 5% [2]. BPD is associated with clinically significant impairments in social, occupational, and other areas of

functioning [5,7,8]. Experts broadly agree on the necessity of specialised interventions and the importance of early treatment to limit deficits in psychosocial functioning [5,9–11]. Various treatment programs for BPD have been developed in the last decades [12–14]. Most of them have been adapted for adolescents. Alongside patients with full syndrome BPD the current study also allows for inclusion of patients who only fulfil a subset of the required criteria to target young patients who present with (yet) milder (sub-threshold) forms. To designate this population the term Borderline Personality Pathology (BPP) is used in the following. At least four manualized therapeutic approaches for

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<https://doi.org/10.1016/j.conctc.2018.10.007>

Received 4 May 2018; Received in revised form 2 October 2018; Accepted 28 October 2018

Available online 31 October 2018

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adolescents with BPP are available: Dialectical Behavior Therapy for Adolescents (DBT-A), Mentalization Based Treatment for Adolescents (MBT-A), Adolescent Identity Treatment (AIT) and Schema-focused Psychotherapy for Adolescents (SFT-A) [15–18].

The effects of different psychotherapeutic approaches can be very similar despite conceptual and practical differences between the models (equivalence paradox or dodo bird verdict) [19]. This effect has been observed in multiple meta-analyses and has led to a paradigmatic shift in psychotherapy research from outcome to process research [20–22]. Pure outcome designs focus on post therapeutic change compared to baseline. Therefore, the actual psychotherapeutic processes remain in a “blackbox”. Change process research is needed alongside randomised controlled trials [23] to understand common and specific factors at work in different types of psychotherapy [20,24]. A better understanding of these factors might help improving therapeutic interventions, designing optimal treatments for specific patient populations and improving the translation of psychotherapeutic models into clinical practice [25,25].

Here, we present the design of a process-outcome study investigating the psychotherapeutic treatment of adolescents with BPP using two specialised approaches: AIT and DBT-A. These approaches differ in their concepts and goals. Psychosocial functioning, that has been shown to be highly impaired in adolescent patients with BPD [26] and presents an important target for health care interventions, has been selected as main outcome variable for the outcome comparison. In accordance with the dodo bird verdict [19], relative equivalence in the improvement of psychosocial functioning due to both DBT-A and AIT is expected.

Beyond this outcome comparison, the psychotherapeutic process is investigated to reach a better understanding of the change mechanisms of AIT and DBT-A. The relative difference of both models regarding their theoretical foundation, bears promise to identify and uncover shared and specific factors. Well investigated generic measures of the psychotherapeutic process as well as more experimental assessments were included in the study design, to cover a broad range of potential variables of interest.

## 2. Methods

The study is registered at [clinicaltrials.gov](https://clinicaltrials.gov) (NCT02518906) [27]. Ethical approval for this study was obtained from the local ethics committees. All adolescents and their therapists provide their written informed consent prior to participation in the trial. Post-trial care is ensured by the local clinical teams.

The methods section first describes the targeted population, the interventions and the setting. The outcome and process questions and methods are outlined in separate sections.

### 2.1. Population

The targeted patients are adolescents with Borderline Personality Pathology (BPP) and identity diffusion, a core symptom of different types of PD [28]. The following inclusion criteria are applied: age 13–19 years;  $\geq 3$  BPD criteria present (assessed with the Structured Clinical Interview for DSM-IV Axis II Personality Disorders, (SCID-II) [29]); identity diffusion (Assessment of Identity Development in Adolescence (AIDA) Total T-score  $> 60$ ) [30]. Exclusion criteria are: an intelligence quotient  $< 80$ ; psychotic disorders; pervasive developmental disorders; severe somatic or neurological disorders; severe and persistent substance addiction; antisocial PD (omitting the age criteria); and necessity of inpatient treatment. The instruments used for determining the inclusion/exclusion criteria are listed in Table 1 under “screening”. Necessity for inpatient treatment was evaluated during screening by a psychiatrist. Both male and female patients are enrolled.

Patients drop out of the study if they require prolonged inpatient treatment ( $> 2$  weeks) beyond short-term crisis intervention, if a

patient does not want to continue the treatment or does not comply to the respective therapeutic framework. Dropouts will be asked to participate in follow-up assessments. To improve participant retention, patients receive a financial compensation. In Basel and Heidelberg patients receive financial compensations after each scientific assessment outside of routine clinical care. The amounts vary according to the length of the respective assessment. In Basel patients receive a total of (the equivalent to) \$400; in Heidelberg \$295. In Santiago the treatment is offered free of charge for study participants. Differences between centres are due to regional economic and health care system differences.

The required sample size for the outcome part was calculated for the primary endpoint at 12 months after baseline using the Clinical Global Assessment Scale (CGAS) [31] (psychosocial functioning) as measure of primary outcome. The sample size calculation assumes a mean CGAS score of 50 points (SD = 7.5) at baseline and 62 points at the primary endpoint. As previously no psychotherapy studies on adolescent BPP patients used psychosocial functioning as primary outcome, these assumptions are based on a landmark study on adolescents with another severe mental disorder (major depressive disorder) by Vitiello et al. [32] which employed the CGAS as primary outcome. Furthermore, it has been assumed that the CGAS scores are multivariate normally distributed (covariance: 0.7). The sample size was calculated based on data simulation. For every sample size  $n_i = 1, \dots, 26 = 10, \dots, 60$ , artificial patient data were generated  $R = 500$  times. To test how the unknown treatment difference between AIT and DBT-A affects the required sample size, the treatment effect of AIT has been varied from 9.3 to 21.3 points. For each simulation, the difference of the treatment success has been estimated together with the 95% confidence interval using a linear model to check whether the confidence interval describing the difference of the two study arms was completely above the predefined margin of  $-7.5$ . Assuming that AIT and DBT-A perform equally well, a sample size of  $n = 23$  patients would be sufficient to have the confidence interval of their difference above the margin of  $-7.5$  in 80% of the cases (power of 0.8). Additionally, expecting a dropout rate of 20%, a sample size of 29 patients per study arm is needed.

### 2.2. Psychotherapeutic interventions and setting

Psychotherapists are psychologists or physicians who underwent or are currently undergoing psychotherapy training to obtain the specialist degree. Additionally, all psychotherapists received specific training for AIT or DBT-A. Regular supervisions of the psychotherapeutic work are taking place at each centre to ensure the psychotherapists' adherence and competence.

#### 2.2.1. Adolescent Identity Treatment (AIT)

AIT [17] is a psychodynamic approach for the treatment of PD in adolescents that integrates modified elements of Transference-Focused Psychotherapy (TFP) [33] with psychoeducation, behaviour-oriented home plans, and work with parents. Like in TFP, the main techniques are clarification, confrontation and interpretation, with an emphasis on the affects in the here and now, as well as the dominant object relationship dyads. During the psychoeducation part of the treatment, both patients and parents are informed about the etiology and course of PD symptoms in adolescents, as well as the specificities of relationship building and maintaining, autonomy, limit setting, and affect regulation in adolescent BPD patients. A written homeplan organizes the overt behavioural interactions between the adolescent and his/her family, provides rewards and consequences for behaviour and clarifies discrepancies of perception between the adolescents and their family. Parents are intensively included in the therapeutic process.

AIT is a manualized outpatient approach. In this study, it contains 25 weekly face-to-face sessions with the adolescents, and 5–8 sessions with their parents. Time points of these parent sessions are planned

**Table 1**  
Outcome instruments.

Type	Instrument	Pre Assessment				Therapeutic Process			Follow-up			
		Screening	Baseline	3rd Session	Before each Session	During each Session	After each Session	Turn of each Month	13 th Session	Post Therapy	12 Months after Baseline	24 Months after Baseline
Pre- and Post Therapy Assessments	Assessment of Identity Development in Adolescence (AIDA)	x								x	x	x
	Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SKID-II)	x								x	x	x
	Wechsler Intelligence Scale for Children (HAWIK) OR Reynolds Intellectual Screening Test (RIST) <sup>a</sup>	x										
	Mini International Neuropsychiatric Interview for Children and Adolescents (MINI-KID)	x								x		
	Children Global Assessment Scale (CGAS) <sup>b</sup>		x							x	x	x
	Columbia Impairment Scale - Parent Version (CIS-P)		x							x	x	x
	Columbia Impairment Scale - Youth Version (CIS-Y)		x							x	x	x
	Clinical Global Impressions Scale (CGI)		x							x	x	x
	School Functioning Rating (SFR)		x							x	x	x
	Beck Depression Inventory II (BDI-II)		x							x	x	
	Childhood Trauma Questionnaire (CTQ)		x									
	Movie for the Assessment of Social Cognition (MASC)		x							x	x	
	KIDSCREEN		x							x	x	
	Levels of Personality Functioning Questionnaire (LoPF-Q 12–18)		x							x	x	
	Strengths and Difficulties Questionnaire (SDQ)		x							x	x	
	Process Research Questionnaires <sup>c</sup>	Parenting Stress Index (PSI)		x							x	x
Borderline Symptom List (BSL-23)			x							x	x	
Self- Injurious Thoughts and Behaviors Interview (SITBI)			x							x	x	x
Zanarini Rating Scale for Borderline Personality Disorder (ZAN-BPD)			x							x	x	
Session Evaluation Questionnaire for the Patient (SEQ)							x					
Session Evaluation Questionnaire for the Therapist (SEQ)							x					
Youth Outcome Questionnaire Self-Report (YOQ-SR)								x		x	x	
Working Alliance Inventory for Patients (WAI)				x						x		
Working Alliance Inventory for Therapists (WAI)				x						x		
Credibility/Expectancy Questionnaire			x									
Parents (CEQ)												
Credibility/Expectancy Questionnaire												
Patients (CEQ)												
Generic Change Indicators (GCI)												x
Ruptures & Resolutions (R&R)												x
Therapist Interventions												x

(continued on next page)

Table 1 (continued)

Type	Instrument	Pre Assessment					Therapeutic Process				Follow-up			
		Screening	Baseline	3rd Session	Before each Session	During each Session	After each Session	Turn of each Month	13 th Session	Post Therapy	12 Months after Baseline	24 Months after Baseline		
Psychophysiology	Electrocardiogram Patient (ECG)		x			x			x	x	x			
	Electrocardiogram Therapist (ECG)					x								
	Electrodermal Activity Patient (EDA)		x			x			x	x	x			
	Electrodermal Activity Therapist (EDA)					x								
	Saliva Cortisol Patient & Therapist				x		x							
	Saliva Cortisol Patient		x							x	x			
	Hair Cortisol Patient		x							x	x			

References of instruments can be seen in Appendix A.

<sup>a</sup> If no other intelligence measure (Wechsler or HAWIE) is available from clinical routine.

<sup>b</sup> Instrument for primary endpoint.

<sup>c</sup> Alliance and expectancy measures were taken at 3rd instead of 1st session to give time to patient and therapist to get to know each other.

according to the needs of the individual patients in accordance with the therapeutic process. Duration of an AIT therapy is 6–8 months approximately, with times of holidays or missed appointments considered.

### 2.2.2. Dialectical behavior treatment for adolescents (DBT-A)

DBT-A [15] is an adaptation of the manualized treatment program DBT that has originally been developed for adults with BPD. While DBT is based on the therapeutic principles of Cognitive Behaviour Therapy, the major modification lies in the integration of Zen Buddhist oriented ideas to accept the specific vulnerabilities of BPD patients as being resistant to change. Thus, the dialectical approach alters between the focus on change of behaviours and attitudes on the one hand, and the focus on accepting the vulnerabilities on the other hand.

In line with the adult version, DBT-A comprises a combination of an outpatient individual therapy and a skills training in groups. For DBT-A, skills taught were modified, with some skills removed and a new module called “Walking the Middle Path” was added to help achieve a balance between validation and change in family environments. Overall, DBT-A includes simplified materials and has a stronger focus on working with caregivers and other systems involved. In this study, DBT-A contains 25 individual sessions as well as 20 sessions of skills training. These sessions are also carried out within 6–8 months.

### 2.2.3. Setting

Recruitment takes place at three centres, each carries out one of the investigated treatment approaches:

- AIT centre 1: Child and Adolescent Psychiatric Hospital of the Psychiatric University Hospitals Basel, Switzerland.
- AIT centre 2: Schilkrut Medical Institute (A. Borzutzky, P. Foelsch) jointly with the Millennium Institute for Research in Depression and Personality, Santiago, Chile.
- DBT-A centre: Clinic of Child and Adolescent Psychiatry, Centre for Psychosocial Medicine, University of Heidelberg, Germany.

### 2.3. Outcome research

Interplay of outcome and process research is illustrated in Fig. 1. The outcome part of the study addresses the following questions: In adolescents suffering from BPP, does an intensive outpatient treatment with the new approach AIT lead to an outcome that is comparable (non-inferior) to an intensive treatment with DBT-A? The non-inferiority design was chosen since DBT-A already has been established as an effective treatment [15,34,35].

Outcome parameters are collected at 4 visits: *Baseline* (before therapy), *Post treatment* (immediately after the end of therapy, time from baseline can vary according to therapy length), a *First Follow-up* (1 year after Baseline, 1yFU) and a *Second Follow-up* (2 years after Baseline, 2yFU). 1yFU is defined as primary end-point. Post Treatment and 2yFU are used to illustrate symptom course and stability of improvement over time.

#### 2.3.1. Outcome parameters

The main outcome criterion is psychosocial functioning, assessed with the CGAS [31]. This scale has a range of 1–100 points, with a score < 10 signifying that the patient needs constant supervision, while a score of > 80 describes a good or even very good level of functioning. For a holistic assessment, secondary outcome parameters represent the domains general psychopathology, personality functioning, borderline specific symptoms, patient's quality of life and stress of the parents. An overview of all outcome parameters is given in the upper part of Table 1.

**Hypothesis A.** AIT is not inferior to DBT-A in terms of improvement in psychosocial functioning.

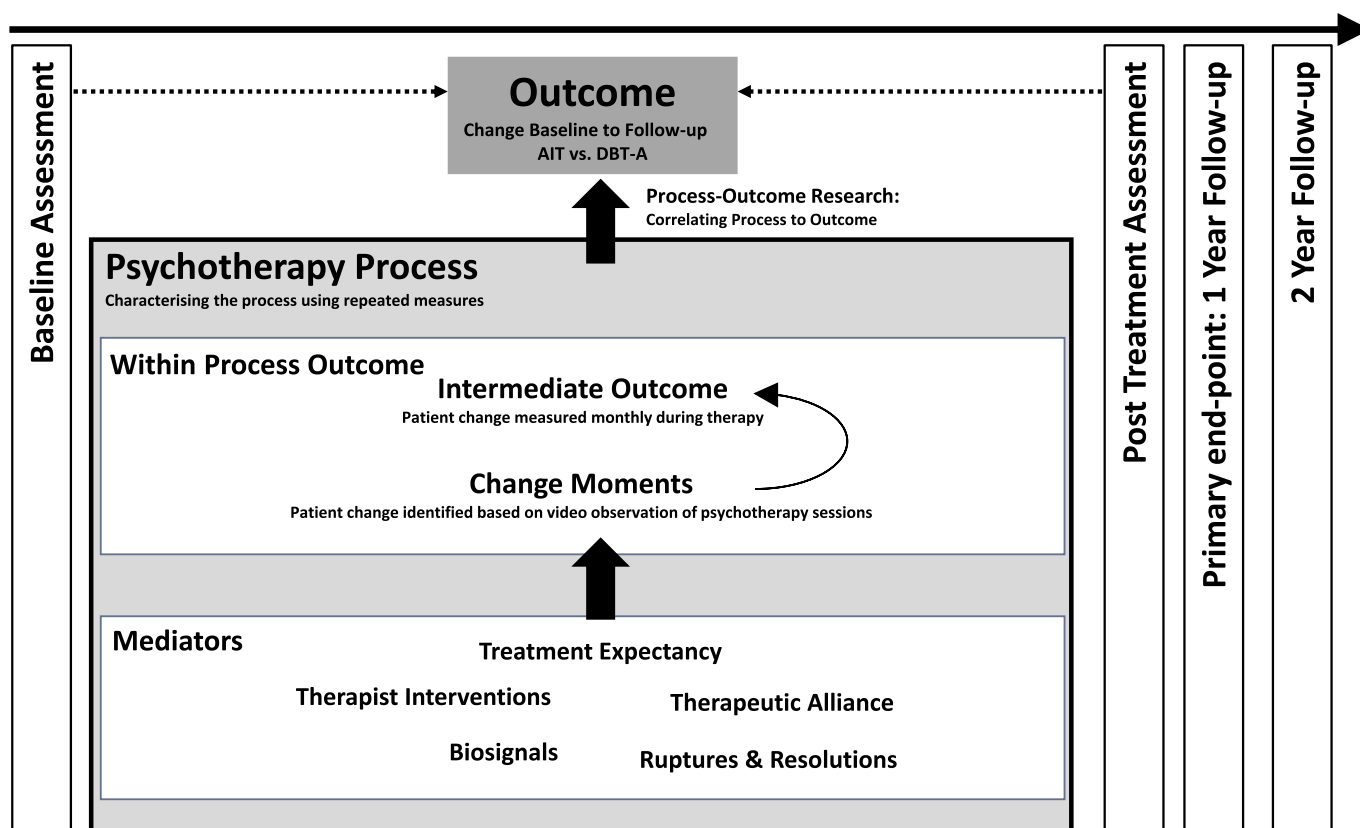


Fig. 1. Combination of outcome- and process-research.

#### 2.4. Process research

The aim of psychotherapy process research is to answer the question “How does psychotherapy work?” [36]. In general, answering this question requires identifying and understanding mechanisms of patient change i.e. how they are brought about by what happens during psychotherapeutic treatment. Before mechanisms can be established it is important to explore the parameters at work. These parameters are not static but considered to vary over time and are, therefore, captured with repeated measures.

Process-outcome research correlates so called mediator variables with outcome. This outcome can consist of “classical” pre-post-outcome parameters such as those described in the previous section. However, to reduce the distance between mediators and outcome and to observe more direct dependencies it is useful to repeatedly evaluate outcome (patient change) throughout the psychotherapeutic process.

##### 2.4.1. Outcome and patient change within the psychotherapeutic process

**2.4.1.1. Intermediate outcome.** Intermediate outcome, defined as the patient's change observed over several sessions of a treatment [37], is monitored with the Youth Outcome Questionnaire Self Rating [38,39] (Y-OQ-SR) on a monthly basis. The questionnaire is constructed to be sensitive to change over short periods of time. It consists of a total distress score and six subscales: interpersonal distress, somatic complaints, interpersonal relations, social problems, behavioural dysfunction and critical items (e.g. hallucinations or suicidal ideas). The Y-OQ-SR is also applied at baseline, post treatment and follow-ups, thus assuring continuity of assessment over the total period of investigation.

**Hypothesis B1.1.** Improvement in intermediate outcome is positively correlated to the (pre-post) overall outcome level.

**Hypothesis B1.2.** Symptoms measured on the intermediate outcome

level decrease throughout psychotherapy.

We are, furthermore, interested in the individual courses of change and how they affect overall psychotherapeutic outcome. In which phase of the therapy do changes occur? Are these changes stable over time or can there be temporary setbacks? A major question of practical relevance is whether early symptom changes predict overall outcome.

##### 2.4.1.2. Patient change in process: the Generic Change Indicators model.

Significant event approaches are considered to be among the promising research strategies to advance the field of psychotherapy process research [19,23]. Change Moments (CM) are significant therapeutic events measured by the Generic Change Indicators model (GCI, [40]). They represent key moments of psychotherapeutic treatment. According to this model, “generic psychotherapeutic change is related to client's transformations on their subjective perspective regarding themselves, their problems and symptoms, and their relationship with the environment in which they occur” [41]. The term “generic” refers to the idea that these change indicators are not limited to certain psychotherapeutic models. Their genericity has been empirically shown [42]. There are 19 sequentially ordered change indicators, which are ordered to represent theoretically necessary steps the patient should take to achieve psychotherapeutic change. The 19 indicators are grouped into the following three stages: 1) Initial consolidation of the therapeutic relationship structure; 2) Increase in permeability towards new understandings; and 3) Construction and consolidation of a new understanding. The validity of this staging model has been empirically confirmed [40]. The model allows capturing changes which happen outside of the psychotherapy sessions (called extra session CM) but which are addressed during psychotherapy. CM are identified based on video analysis of all psychotherapeutic sessions by independent trained observers. It is important that non-verbal as well as verbal behaviour is taken into account for valid rating. As shown previously [40] in other patient



samples CM are correlated to outcome.

**Hypothesis B2.1.** CM are positively correlated to intermediate and overall outcome.

**Hypothesis B2.2.** Total number of CM is less strongly correlated to outcome than a progression from lower level CM to higher level CM, which represents the passing through (according to the model) necessary steps of psychotherapeutic change.

#### 2.4.2. Mediators of therapeutic change

**2.4.2.1. Psychotherapeutic alliance.** Psychotherapeutic alliance is among the most studied common factors in psychotherapy and robustly predicts psychotherapeutic outcome [43]. Patients with personality disorders have difficulties to develop stable interpersonal relationships, which also affects the psychotherapeutic alliance [44]. Therefore, psychotherapeutic alliance can be hypothesised to be a central mediator variable of psychotherapeutic outcome in these patients.

The Working Alliance Inventory (WAI; [45]) conceptualises alliance in terms of agreement on goals, task and bond. It is filled out before the 3rd, 12th and final sessions by both, patients and therapists.

**Hypothesis B3.1.** Working alliance is positively correlated to intermediate outcome.

**Hypothesis B3.2.** Working alliance is positively correlated to improvement in overall outcome.

**2.4.2.2. Ruptures and resolutions (R&R).** To come to a deeper understanding of therapeutic alliance, the R&R model is applied. The R&R model conceptualises alliance as a dynamic phenomenon [46] and is based on video ratings of psychotherapeutic sessions. Ruptures are deteriorations in the quality of the therapeutic relationship. They represent inevitable interpersonal events [47,48]. Ruptures are conceptualised to put into effect dysfunctional interpersonal patterns and, therefore, are a window to work on these patterns [48]. Ruptures are organised into two classes: withdrawal and confrontation. In withdrawal ruptures, the patient disengages from the therapeutic process and/or the therapist (e.g. falling silent). In confrontational ruptures, the patient directly expresses anger or dissatisfaction towards the therapist or the treatment. In the model, the therapist can react to rupture episodes using resolution strategies. In the present study, R&R episodes will be rated by trained observers according to the “Rupture Resolution Rating System (3RS): Manual” based on video recordings of the psychotherapeutic sessions [49]. According to the R&R model, it is possible that ruptures and their resolutions promote occurrence of change. Based on the results of [50] who also investigated R&R in young patients with BPD, we hypothesise that:

**Hypothesis B4.1.** The occurrence of alliance ruptures follows an inverted u-shaped trajectory across treatment time. This pattern indicates intensive and frequent alliance ruptures during the middle phase of the treatment.

**Hypothesis B4.2.** Intensive and frequent early ruptures are negatively correlated to overall outcome.

Finally, sequence analyses of R&R and CM are of special interest [23,51] to understand the effect of R&R in the occurrence of psychotherapeutic change.

**2.4.2.3. Treatment expectancy.** Treatment expectancy plays a key role in the process and outcome of psychotherapy [22,52,53]. Empirical support for its importance also comes from placebo research. The placebo effect is regarded as a well-founded psychobiological phenomenon in which improvement in symptoms is explained by the meaning and expectancy a patient attributes to the treatment [54–57].

BPD is difficult to treat and patients often have an ambiguous relationship with the health care system based on multiple negative experiences in former psychotherapies. Treatment expectancy might be a crucial variable to address in the treatment of these patients. In the present study, patients and parents are asked about their treatment expectancy at the beginning and the 12th session (patients only) of treatment. We apply the Credibility and Expectancy Questionnaire (CEQ) (Deville & Borkovec, 2000) which is a short self-report questionnaire that consists of two factors, the cognitively based credibility and the affectively based expectancy for treatment. The credibility items ask how logical the offered therapy seems, how successful patients think it will be, and how confident they are in recommending it to others. The expectancy items ask how much improvement they expect, how much they really feel it will help, and how much improvement they really feel will occur.

**Hypothesis B5.1.** Higher treatment expectancy is correlated with better overall outcome.

**Hypothesis B5.2.** Higher treatment expectancy is correlated with better early working alliance (measured by WAI, as well as R&R).

**2.4.2.4. Therapist interventions.** From a clinical perspective, the investigation of therapist interventions and the use of psychotherapeutic techniques are of high relevance. However, psychotherapy research has often failed to provide evidence for the link between therapeutic model and outcome [19,58]. Based on this experience, psychotherapy research moved away from investigating broad comprehensive models, instead looking at what happens on a restricted timescale aiming at constructing therapeutic models bottom up. A further research problem is that psychotherapeutic interventions do not work based on a dose to effect–response logic but rather seem to depend on an adequate “responsiveness” [58], implying the therapist's good timing, intuition, empathy as well as interactivity with the patient [59]. It is of relevance to address the questions of therapist interventions from a bottom up perspective in this sample as patients with BPD are reckoned to be difficultly treated. The questions are “what works in these patients and where are potential pitfalls?”.

Therapist interventions will be assessed from a generic, trans-theoretical perspective, at the level of significant events (CM and R&R) (i.e. speaking turns before, during and after these events). First, primary therapist response modes (question, advisement, information, reflection, interpretation, and self-disclosure) will be evaluated. To measure these techniques, we will use the ‘Techniques’ dimension of Therapeutic Activity Coding System (TACS) [60]. Additionally, we will use the three main ‘Communicative Intentions’ from the TACS (exploring, attuning and resignifying) [61] jointly with the three main AIT techniques (clarification, confrontation and interpretation) [17].

To address the problem of responsiveness, alliance will be investigated as a potential mediator of employed interventions [62]. Further mediators of the relation of significant events and interventions will be the progression of the psychotherapeutic work in terms of time (number of session) as well as attained level of the change indicators.

**Hypothesis B6.1.** Use of therapist interventions is mediated by alliance.

**Hypothesis B6.2.** Use of therapist interventions is mediated by progression of therapy (time in therapy).

**Hypothesis B6.3.** Use of therapist interventions is mediated by the level of change CM.

#### 2.5. Biological markers

In this study, electrocardiogram (ECG) and electrodermal activity (EDA) are measured in patients and therapists in the psychotherapy

sessions as well as during resting state. Saliva cortisol is measured in patients and therapists before and after each therapy session, hair cortisol in patients at pre- and post-assessment. The biological markers are investigated for their potential to inform about relevant aspects of the psychotherapeutic process as well as in correlation to patient change.

During the psychotherapeutic sessions patients and therapists are equipped with wearable ECG and EDA devices. Single lead surface ECG with a fixed potential ground electrode was recorded from both patient and therapist using Ag/AgCl electrodes (Kendall H135SG) with a Shimmer ECG devices [63]. The first electrode was placed directly under the centre of the right clavicle. The ground electrode was placed 3–5 cm below the first electrode. The second electrode was placed at the same level as the ground electrode below the centre of the left clavicle. This procedure was chosen so that patient and therapist were able to attach the ECG device on their own and to avoid undressing of the participants. The ECG signal was sampled at 1024 Hz. Electrodermal Activity was assessed using shimmer3 GSR + devices that monitor activation of sweat glands via two reusable electrodes attached to the index and middle finger of the non-dominant hand. In Heidelberg, ECG were recorded using an ekgMove 3 sensor (movisens GmbH, Karlsruhe, Germany) attached to the participants chest at the base of the sternum using a flexible belt with two integrated electrodes that were watered before the recording. ECG signals were recorded at a sampling rate of 1024Hz. The devices are synchronised to each other and to the video signal. Saliva cortisol of both, patient and therapist, is taken at the beginning and end of each session. Resting state measures of all biological markers are taken at baseline, mid therapy and follow-up visits (see Table 1).

#### 2.5.1. Biological markers of outcome

A first question of interest is whether systematic changes of the investigated biological markers can be observed over the psychotherapeutic process and in the follow-up resting state visits compared to the baseline assessments. While heart rate variability (HRV) is correlated with borderline personality symptom severity in adolescents [64] its change over the psychotherapeutic process has, furthermore, been correlated to change in these symptoms [65]. This cardiac marker might, therefore, be useful to track psychotherapeutic outcome in adolescents with BPP. Similarly, the cortisol and electrodermal responses have been found to be altered in correlation to borderline personality symptoms [66–69] and might change under psychotherapeutic treatment.

**Hypothesis C1.1.** Increase in HRV over the course of the psychotherapy is correlated to better overall outcome.

**Hypothesis C1.2.** Decrease of cortisol response over the course of the psychotherapeutic treatment is correlated to better overall outcome.

#### 2.5.2. Biological markers and significant therapeutic events

A second aim is to characterise these biological markers in correlation to significant therapeutic events (CM and R&R). In analogy to the Therapeutic Cycle Model [70,71], which states that psychotherapeutic change is facilitated by appropriate cognitive and emotional circumstances, we hypothesise that patient's changes are facilitated under certain physiological conditions, which can be characterised by the proposed biomarkers.

**Hypothesis C2.1.** CM are more likely under certain conditions which can be characterised by biological parameters.

**Hypothesis C2.2.** R&R are more likely under certain conditions which can be characterised by biological parameters.

#### 2.5.3. Interpersonal physiology

A further question of interest is interpersonal physiology [72]

during psychotherapy i.e. in this case the synchrony of patient and therapist biosignals. It can be studied in a multitude of modalities (e.g. psychophysiology, vocal frequency, motion energy analysis [73]) and has been related to psychotherapeutic alliance [74]. For example, concordance of EDA has been shown to be correlated to patient perceived empathy of psychotherapists [75]. The phenomenon of interpersonal physiology is an important upcoming topic in psychotherapy research. It might be a basic mechanism of psychotherapy in which patient and therapist have to create a shared psychotherapeutic space.

**Hypothesis C3.1.** Synchrony of biosignals is correlated to alliance.

**Hypothesis C3.2.** Synchrony of biosignals is correlated to overall outcome.

### 3. Discussion

The presented design investigates the outcome and process of psychotherapy in adolescents with BPP:

#### 3.1. Outcome research

“Classical” outcome research with psychosocial functioning as primary end-point answers the question of the efficacy. The end-point has been chosen as a fair comparator between the quite different psychotherapeutic models and is arguably one of the most relevant and generally valid treatment targets in this sample of adolescents.

In this outcome comparison, the allocation of the patients is not randomised. Randomised controlled trials (RCT) have important advantages in reducing statistical biases [76]. There are, however, detriments to RCTs: The efficacy-effectiveness gap [77,78] describes the difference of performance under research (efficacy) and everyday clinical practice (effectiveness) conditions [79]. This gap is important to take into consideration. With the presented study design, we undertake the evaluation of a clinical intervention in a specific set of patients (adolescents with BPD) thus being obliged to use a multicentre design to guarantee sufficient sample size, and the treatment approaches described (AIT and DBT-A) are run in naturalistic settings, i.e. the involved centres are specialized in the application of the respective interventions. This gives our study, which also investigates the therapeutic process, more ecological validity compared to a standard RCT. In contrast, in order to implement a RCT, it would be necessary to make both psychotherapeutic models available at all study centres. However, psychotherapeutic formation is an expensive process and due to the required investment psychotherapists tend to select the psychotherapeutic formations based on personal attitudes and beliefs. A possible solution could be the relocation of the psychotherapists. However, this would multiply the costs of the clinical trial and, additionally, the setting would be still artificial in contrast to the routinely implemented psychotherapies. Consequently, we decided to let the interventions be carried out in the respective specialised centres, thus profiting from an “adversarial collaboration” [80] to implement a fair and balanced study design. In this case, allocation to the study arms was decided on by recruitment location. Despite the application of identical inclusion criteria, the multicentre nature of the study might result in differences between the three samples (e.g. severity of symptoms, ratio of male to female patients, age) which might be related to study site specifics. Statistical control for such effects is necessary. Additionally, while the recruitment from specialised settings is necessary for the feasibility of the study, it also might limit generalisation of the results to other (less specialised) contexts.

#### 3.2. Process research

The process part of the study aims at researching the question of how therapy works. It relies on multiple approaches (i.e. measuring

intermediate outcome, evaluating expectancy and alliance from the patient and therapist points of view), identifying significant therapeutic events (R&R and CM) as well as analysing micro process (therapist interventions and psychophysiology).

This “systematic methodological pluralism” is intended and recommended for psychotherapy research [23,40]. Kazdin [25] points out the importance of repeated application of instruments over the psychotherapeutic process as a means of establishing mechanisms of psychotherapeutic functioning in the sense that the mediator variables should change before the outcome variable. The focus on clinical realities should help narrowing the evident gap between research and practice in psychotherapy [19,81].

Hierarchical and latent variable modelling are options to address the problem of multiple levels and timescales in the data set resulting from this study design. It is our goal to not only observe inter-individual differences, but also to consider intra-individual changes over time. Thus, the time variable will be used as a quantitative variable in these models to describe and understand the timely interdependence of the observed process phenomena and their impact on the outcome variables. The sample size might in certain regards prove as one of the major limitations of this study. Results will be partially explorative in nature. However, this limitation should not prevent researchers from addressing relevant questions. The field is relying on and developing a number of data analytic instruments such as qualitative research [82], case studies, time series and sequence analysis or methods derived from dynamic systems theory [83].

An important aspect in studying the psychotherapeutic process is considering external factors which can interact with the psychotherapy. While external factors are considered in the present design by assessing extra session change indicators, it is still possible that important external factors are missed.

The implementation of the psychotherapy research framework can burden the patients, the therapist and bias the therapeutic process. Our impression is that video recordings are well tolerated by patient and therapist and are quickly assimilated into normality. However, video-based observer ratings are very costly. For psychophysiological data collection wearable devices were used. These were also well accepted. It is important that a research collaborator and not the psychotherapist is responsible for the mounting of these devices and the research procedures in general to maintain an as high as possible ecological validity.

## Declarations

### Ethics approval and consent to participate

Ethical approval for this study were obtained locally:

- In Basel: Ethikkommission Nordwest-und Zentralschweiz (Reference: EKNZ 2015-230)
- In Heidelberg: Ethics commissions of the Medical Faculty, University of Heidelberg (Study: ID S-425/215)
- In Santiago de Chile: Scientific Ethics Committee of Social Sciences, Arts and Humanities, Pontifical Catholic University of Chile (Fondecyt N°3130367)

### Consent for publication

Not applicable.

### Availability of data and material

Requests regarding the further use of this dataset or parts of the data are very welcome. Availability will be decided on in consultation with the respective study centres. Please direct any requests to the corresponding author.

## Competing interests

Klaus Schmeck and Susanne Schlüter-Müller are co-authors of the Manual of Adolescent Identity Treatment (AIT).

## Role of the funding source

Basel: The study is funded by the University of Basel and the Psychiatric Hospitals of the University of Basel.

Heidelberg: the study received no external funding by any third party.

Santiago: The study is funded by both, Schilkrut Medical Institute and Millennium Institute for Research in Depression and Personality (MIDAP). Additionally, the study was supported by the Millennium Science Initiative of the Ministry of Economy, Development and Tourism, Project IS130005.

## Trial registration

The study has been registered on 10th August 2015 at clinicaltrials.gov (NCT02518906). The current paper does not contain empirical results.

## Acknowledgements

We would like to thank the participating patients and psychotherapist for trusting us with the scientific analysis of their psychotherapeutic work. Furthermore, we would like to thank the Clinical Trial Unit Basel for help with the ethics approval and the non-inferiority design.

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